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Pingelap and Mokil Atolls: Achromatopsia

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Congenital achromatopsia with high myopia has a frequency of several percent among the inhabitants of Pingelap Atoll, Ponape District, U.S. Trust Territory of the Pacific Islands [1]. Pedigrees suggest an autosomal recessive gene which reached high frequency after Typhoon Lengkieki devastated the atoll around 1775 [2]. Ethnohistorical, epidemiological, and genetic evidence on this hypothesis will now be presented.

ETHNOHISTORY

Four field trips to the Ponape District during 1969–1970 and later interviews with Pingelapese informants in Honolulu led to rather complete genealogies and several ethnohistorical accounts of achromatopsia. One survivor of Typhoon Lengkieki, the Nanmwarki Mwahuele, is the ancestor through three wives of all known carriers among Pingelapese and the neighboring Mokilese (table 1). The ethnohistory of achromatopsia is concerned with three descendant sibships (fig. 1).

TABLE 1

KINSHIP OF CARRIER SIBSHIPS TO SIBSHIP 1067

	KINSHIP TO 1067		
	No	Yes	Total
Not a known carrier	363	727	1,090
Known carrier	0	117	117
Total	363	844	1,207

The Nanmwarki Okonomwaun who ruled from 1822–1870 took the Pingelapese wife of a Kusaiean immigrant [2]. By this woman, Dokas, he had six children, of whom two had achromatopsia. They were explained by the following myth. The god Isoahpahu became enamored of Dokas and instructed Okonomwaun to appropriate her. From time to time, Isoahpahu appeared in the guise of Okonomwaun and had intercourse with Dokas, fathering the affected children, while the normal children came from Okonomwaun. Isoahpahu

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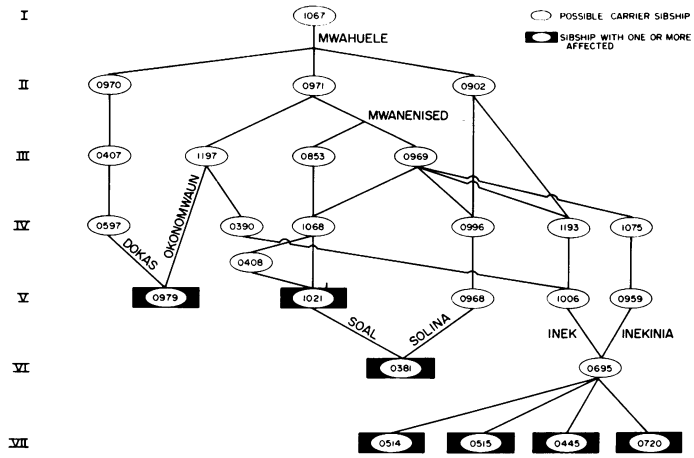

FIG. 1.—Ethnohistory of achromatopsia

loved other Pingelapese women and had affected children by them. The "proof" of this is that persons with achromatopsia shun the light but have relatively good night vision, like their ghostly ancestor. Isoahpahu was prominent in the Pingelapese pantheon until overthrown by the missionaries. He is said to have fled in shame when defeated in a test of supernatural power, and his house was destroyed.

Soal was the oldest patient with achromatopsia seen by our most elderly informants. Descended from the Nanmwarki Mwanenised by an uncle-niece mating, he married another descendant of Mwanenised and had six children, of whom three were affected. One of the normal daughters went to Mokil, a neighbor island, and was the ancestress of several sibships with affected children. Imwerou, one of Soal's affected sons, learned witchcraft from other Micronesians in the phosphate mines of Nauru. He was held in some awe by the Pingelapese and Mokilese. George Higgins, the Nahnkin of Mokil, relates how Imwerou prophesied that the first player in a game of stick throwing would have bad luck. George Higgins ignored this warning and threw first. That night one arm was paralyzed by a polio-like disease which killed or crippled many of the workers on Nauru. When the arm remained weak he accused Imwerou of witchcraft. Imwerou admitted his responsibility and prepared an herbal potion which promptly cured his patient-victim. Imwerou did not have children. His stepson is a Christian minister, who seldom displays the mystic arts he is generally believed to have learned from Imwerou.

Married couples baptized by the missionaries often received names like Soal and Solina. One such couple, also descended from Mwanenised, was Inek and Inekinia. Inek was trained in the Christian faith by Mesdon (Mr. Doane) and assigned to Truk, but he refused because of his large family. According to Pingelapese legend, Mesdon was angered by this lack of evangelical zeal and cursed the children, four of whom subsequently had affected offspring. In all, seven of Inek's grandchildren had achromatopsia.

These legends reflect prevailing attitudes. The night vision of affected persons excites some awe, but there is a definite stigma attached to the disease. One contemporary couple who had two affected children named their first normal son Aringado (from a Japanese word meaning "thanks"). Achromatopsia interferes with activities requiring good vision in bright sunlight, most of which are traditionally men's work like fishing and picking breadfruit. Bad vision often leads to cuts and bruises. Work in the taro pit and at home is much less impaired, and success in a clerical job is possible. Nevertheless, there is prejudice against marriage to an affected person because of risk to the children. Affected girls who remain unmarried may have one or more illegitimate children.

SEX, AGE, AND INCIDENCE

The frequency of males among examined affected is .4561, which compares closely with the rate for normals, .4796 (table 2). Among reported affected, there is a nonsignificant excess of males, which may reflect the more conspicuous impairment of males.

TABLE 2

SEX DISTRIBUTION

	Sex		
	Male	Female	Total
Examined, affected	26	31	57
Not examined, affected	15	8	23
Examined, not affected	470	510	980

Symptoms of achromatopsia are present after the first 2 months of life. There is no effect on survival. Parents take as good care of affected as of unaffected children, and there is no evidence that this was not so in the past. Affected are homogeneously distributed over age groups (table 3). A deficiency of affected children

TABLE 3

	Age Distribution									
	0–4	5–9	10–14	15–19	20–29	30–39	40–49	50–59	60–90	Total
Examined, affected	5	12	11	9	9	1	6	2	2	57
Examined, not affected	208	226	195	106	125	97	88	80	78	1,203
Total	213	238	206	115	134	98	94	82	80	1,260

aged 0–4, as described by Brody et al. [3], could not be confirmed ($\chi_1^2 = 2.81$).

We examined a total of 57 affected among Pingelapese and Mokilese on the atolls and on Ponape (table 4). It is very likely that, in the district center, we preferentially examined affected, and so we have based our incidence estimates on the atoll populations. The incidence for Pingelapese affected is 4.91%, considerably higher than Mokilese, with 0.56%. Evidence that Mokilese cases are descended from Pingelapese carrier migrants has been presented elsewhere ([2], fig. 1). Pedigree information from sibships with at least one examined member gave an incidence estimate of 5.37% for Pingelapese and 1.04% for Mokilese (table 5). Using historical information, there were no affected Pingelapese in the first three generations after Typhoon Lengkieki. The incidence rose to 2.70% in generations 4–5 and to 4.92%

TABLE 4

INCIDENCE AMONG EXAMINED INDIVIDUALS

Population	Affected	Normal	Total	Incidence (%)
Pingelap	28	542	570	4.91
Pingelapese on Ponape	22	141	163	...
Mokil	2	357	359	.56
Mokilese on Ponape	5	168	173	...

TABLE 5

INCIDENCE IN PEDIGREES

	Affected	Normal	Total	Incidence (%)
Sibships with examined member:				
Pingelapese	60	1,058	1,118	5.37
Mokilese	7	665	672	1.04
All sibships:				
Pingelapese, generations 1–3	0	211	211	0
Pingelapese, generations 4–5	18	649	667	2.70
Pingelapese, generations 6–9	69	1,333	1,402	4.92
Mokilese, generations 6–9	7	699	706	0.99

in generations 6–9, which compares well with the incidence estimate of 4.91% among examined Pingelapese on Pingelap. For Mokilese, the incidence in pedigrees is zero before generation 6 and 0.99% thereafter. Thus, roughly 5% of the Pingelapese and 1% of the Mokilese population are affected.

SEGREGATION ANALYSIS

Since our estimates of incidence from population and pedigree observations agreed closely, we took $\pi = 1$ for contemporary data and $\pi = .5$ for historical data. Analysis under the null hypothesis of a recessive trait without sporadic cases showed a good fit (table 6).

We submitted the Pingelapese data to complex-segregation-analysis models as developed by Falconer [4], Edwards [5], and Morton et al. [6]. Consider a gene G with frequency q which determines risks $t + z$, $td + z$, and z in the genotypes GG, GG', and $G'G'$, respectively, where d is the dominance of G and t is the penetrance. Let A be the incidence. Maximum-likelihood analysis takes the parameters A, d, t, and $x = z/A$.

Under the single locus model with the null hypothesis of $t = 1$, $d = 0$, and $x = 0$, the likelihood ratio χ^2 was 115.42, df = 174 (table 7). Iteration for x was nonsignificant, in agreement with evidence from segregation analysis. We obtained a better fit by iterating for t with $\chi^2 = 108.63$ ($t^* = .662$). Under this hypothesis,

TABLE 6

SEGREGATION ANALYSIS, INCOMPLETE SELECTION

GENERATION	NO. AFFECTED PARENTS	H_0			U SCORES		K MATRIX		
		p	x	π	U_p	U_x	K_{pp}	K_{px}	K_{xx}
4–6	0	$\frac{1}{4}$	0	.5	−25.03	18.62	293.6	−92.9	56.7
7–9	0	$\frac{1}{4}$	0	1.0	−14.66	−13.01	699.0	−348.4	470.2
4–6	1	$\frac{1}{2}$	0	.5	−4.53	−4.70	65.4	−57.9	676.4
7–9	1	$\frac{1}{2}$	0	1.0	−11.11	−4.78	61.0	−78.3	590.0
Total	...	...	...	...	−55.33	−3.87	1,119.0	577.5	1,793.3

TABLE 7

COMPLEX SEGREGATION ANALYSIS OF ACHROMATOPSIA ($A = .0491$)

PARAMETERS	RECURRENCE RISKS IN SIBS			RECURRENCE RISKS IN CHILDREN		LIKELIHOOD RATIO	
	$h = 0$	$h = 1$	$h = 2$	$h = 1$	$h = 2$	χ^2	df
Single-locus model 1:							
$d = 0, t = 1, x = 0$	.250	.500	1.000	.181	1.000	115.42	174
$d = 0, t = 1\text{-}xA, x^* = .093$	.225	.489	.982	.166	.859	112.99	173
$d = 0, x = 0, t^* = .662$	.205	.368	.662	.155	.662	108.63	173
$x = 0, t = 1, d^* = .016$	.232	.467	.945	.175	.898	113.83	173
$d = \frac{1}{2}, t = 1\text{-}xA, x^* = .180$	.194	.292	.490	.234	.440	116.53	173
$d = \frac{1}{2}, x = 0, t^* = .645$	.185	.213	.357	.190	.347	113.31	173
$d = \frac{1}{2}, x^* = .067, t^* = .704$	.183	.226	.377	.195	.356	113.08	172
$d = 1, x = 0, t^* = .339$	.189	.194	.263	.185	.261	113.59	173
Skellam model 2:							
$t^* = .238$	...	.238	...	.049	...	126.07	173
Quasi-continuity model 3:							
$t^* = .999$	.127	.346	.716	.214	.700	116.40	173

the recurrence risk in sibships with one affected was .205, which, in conjunction with a reduced estimate of t, gives evidence for misclassification of affected, probably due to neonatal deaths, and for the popular tendency to attribute affected children to affected fathers.

With Falconer's quasi-continuity model, the heritability was estimated as .999 and the likelihood ratio χ^2 was 116.40, which exceeds by 7.8 the best-fitting single-locus hypothesis of rank 1.

DISCUSSION

Discrimination between single-locus and multilocus hypotheses is moderate. The incidence of achromatopsia with high myopia ($A = .0491$) is at least 100 times

greater than in other populations. If we submit the above data under incomplete selection with $A = .000491$, the likelihood ratio χ^2 for quasi-continuity exceeds by 13.6 its value for a recessive hypothesis. Thus, better discrimination is obtained for rare traits.

Other evidence for a recessive hypothesis is obtained from ethnohistorical reports relating the drastic reduction of the population 200 years ago. The best evidence, however, is obtained from pedigree analysis, which traces all known affected to a single survivor of Typhoon Lengkieki [2].

SUMMARY

Congenital achromatopsia with high myopia has an incidence of 5% among the Pingelapese and 1% among the Mokilese, originating from two neighboring islands in the Ponape District, U.S. Trust Territory of the Pacific Islands. Pedigrees suggest an autosomal recessive gene, which reached high frequency after Typhoon Lengkieki devastated the atolls around 1775. Rather complete genealogies and several ethnohistorical accounts identify one survivor of Typhoon Lengkieki, the Nanmwarki Mwahuele, as ancestor through three wives of all known carriers, including three migrants to Mokil. The sex ratio among affected compares closely with that for normals. Affected are homogeneously distributed over age groups.

Segregation analysis under the null hypothesis of a recessive trait without sporadic cases gives a good fit. Submitting the data to complex-segregation-analysis models, discrimination between the best-fitting single-locus hypothesis of rank 1 and a quasi-continuity model is obtained with a difference in likelihood ratio χ^2 of 7.8. Better discrimination would be obtained if the trait were rarer, but pedigree analysis provides the best evidence for monogenic recessivity.

REFERENCES

1. Carr RE, Morton NE, Siegel IM: Achromatopsia in Pingelap Islanders: study of a large genetic isolate. *Amer J Ophth* 72:746–756, 1971
2. Morton NE, Hurd JN, Little GF: Pingelap and Mokil Atolls: a problem in population structure. In preparation
3. Brody JA, Hussels I, Brink E, et al: Hereditary blindness among Pingelapese people of Eastern Caroline Islands. *Lancet* 1:1253–1257, 1970
4. Falconer DS: The inheritance of liability to certain diseases, estimated from the incidence among relatives. *Ann Hum Genet* (London) 29:51–76, 1965
5. Edwards JH: Linkage studies of whole populations, in *Proceedings 3d International Congress Human Genetics,* edited by Crow JF, Neel JV. Baltimore, Johns Hopkins Press, 1967, pp 483–489
6. Morton NE, Yee S, Lew R: Complex segregation analysis. *Amer J Hum Genet* 23: 602–611, 1971